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|---------------------------------|-------------|----------------------|---------------------|--------------------|
| 09/762,568 | 07/30/2001 | Atsushi Katsumanta | HIKARI.001APC | 5060 |
| 20995 | 7590 | 06/01/2004 | EXAMINER | |
| KNOBBE MARTENS OLSON & BEAR LLP | | | | SULLIVAN, DANIEL M |
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| IRVINE, CA 92614 | | | | 1636 |

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

| | |
|-------------------|-------------------|
| Application No. | KATSUMANTA ET AL. |
| Examiner | Art Unit |
| Daniel M Sullivan | 1636 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 29 April 2004.
2a) This action is **FINAL**. 2b) This action is non-final.
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,2,4-8 and 15-18 is/are pending in the application.
4a) Of the above claim(s) 16-18 is/are withdrawn from consideration.
5) Claim(s) 1 and 5-7 is/are allowed.
6) Claim(s) 2,4,8 and 15 is/are rejected.
7) Claim(s) _____ is/are objected to.
8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
10) The drawing(s) filed on 29 April 2004 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) Notice of Informal Patent Application (PTO-152)
6) Other: _____

DETAILED ACTION

This Office Action is a reply to the Paper filed 29 April 2004 in response to the Non-Final Office Action mailed 26 November 2003. Claims 9-14 and 16-18 were withdrawn from consideration and claims 1-8 and 15 were considered in the 26 November Office Action. Claims 3 and 9-14 were canceled and claims 1, 2, 4-8 and 15 were amended in the 29 April Paper. Claims 1, 2, 4-8 and 15-18 are pending and claims 1, 2, 4-8 and 15 are under consideration.

Election/Restrictions

Applicant's right to rejoinder of the process claims 16-18 upon allowance of the product claim 2, from which they depend, is acknowledged. Applicant is reminded that in the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Further, withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Response to Amendment

Rejection of claim 3 is rendered moot by cancellation of the claim.

Priority

Perfection of a priority claim under 35 U.S.C. §119 (a)-(d) by the filing of a corrected application data sheet is acknowledged

Drawings

The substitute drawings are approved by the Examiner.

Specification

Objection to the disclosure as lacking a descriptive title is withdrawn in view of the amendment to the title.

Claim Objections

Objection to claim 8 as encompassing non-elected subject matter is withdrawn.

Claim Rejections - 35 USC § 101

Rejection of claim 8 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of the amendment of the claim such that it is now directed to a cell.

Claim Rejections - 35 USC § 112, first paragraph

Claims 8 and 15 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter for reasons of record and herein below in the response to arguments.

Claim Rejections - 35 USC § 112, second paragraph

Rejection of claims 1, 2, 4-8 and 15 under 35 U.S.C. 112, second paragraph, as being indefinite for reasons of record is withdrawn in view of the amendments and arguments filed 29 April.

Claim Rejections - 35 USC § 102

Rejection of claims 1, 2 and 6-8 under 35 U.S.C. 102(b) as being anticipated by either one of Panganiban *et al.* (1983) *Nature* 306:155-160 or Panganiban (1984) *Cell* 36:673-679 is withdrawn in view of the amendment of the claims such that they are now limited to comprising an integrase recognition region comprising a connecting sequence of terminal bases formed when one LTR is joined to another LTR.

Rejection of claims 1, 2 and 8 under 35 U.S.C. 102(b) as being anticipated by VonMelchner *et al.* (WO 97/07223) is withdrawn in view of the limitation of the plasmid vector to comprising a retroviral integrase gene.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 8 and 15 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transformant transformed with the plasmid according to claim 2, wherein said transformant is an isolated host cell or a transgenic chicken expressing a GFP transgene, and a method of producing a useful substance in a host cell *in vitro* or producing GFP in a transgenic chicken, does not reasonably provide enablement for transgenic animals, or methods of using transgenic animals, other than a transgenic chicken expressing a GFP.

With regard to claim 8, as amended, Applicant argues that one of skill in the art, even without the teaching in the present specification, would know how to transform any type of cell with a vector to produce a cell transformed by the vector. This argument has been fully considered but is not deemed persuasive. In the paragraph bridging pages 44-45, the specification states, “[e]xamples of host cells into which the vectors of the present invention can be introduced include...cells in living plants or animals.” Although the skilled artisan might be able to make a cell in a living plant or animal which contains the vector, the only uses contemplated in the specification for such cells in a plant or animal are the production of a useful substance and gene therapy. For reasons set forth in the previous Office Action and herein below, the specification fails to teach the skilled artisan how to make the cell in living plants and animals such that it can be used for the purposes set forth in the specification. Therefore, the claimed cell is not enabled beyond the scope of cultured cells.

Regarding enablement for the method of claim 15, Applicant argues that practicing the full scope of the claimed method would require only that the skilled artisan identify a gene of interest and clone the gene of interest operably linked to a promoter into the plasmid in such a

way that it will be expressed once integrated. Applicant urges that the skilled artisan would be easily able to identify and clone an expressible gene of interest into the plasmid. This argument has been fully considered but is not deemed persuasive. Applicant seems to be arguing that all that is required to obtain useful expression of a gene of interest is to clone said gene of interest into the vector and introduce the construct into a cell. However, this argument completely ignores the many obstacles to obtaining useful expression of a gene of interest *in vivo* beyond introducing a nucleic acid into a cell, which were described in detail in the previous Office Action. For reasons provided in that Office Action, it would not be possible to obtain useful expression of the vast majority of genes of interest according to the claimed method. Therefore, the skilled artisan would have to experiment unduly to distinguish which embodiments of the claimed method would be operative.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole. Therefore, the claims stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for the full scope of the claimed subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 8 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

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described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 2 has been amended to recite that the vector of claim 1 further comprises a gene of interest. In support of the limitation “gene of interest”, applicant urges that the term is known and understood by one of skill in the art. However, Applicant does not indicate where in the specification explicit or implicit support for the limitation can be found. The closest support that the Examiner can find is in the second full paragraph on page 44 of the specification, which states, “[a] vector is prepared by inserting as the DNA segment (D4) a segment of DNA encoding a useful protein”. Thus, D4, as contemplated in the specification, is limited to a segment of DNA encoding a useful protein, while one of ordinary skill in the art would understand a gene of interest could encode nucleic acids such as antisense RNA’s or catalytic RNA’s which do not encode a protein. Thus, the originally filed specification does not provide support for the full scope of a gene of interest as the skilled artisan would understand the phrase.

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a)

the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claim is directed to a plasmid vector construct comprising a segment of DNA forming a region for controlling the expression of the integrase gene situated within the connecting sequence of terminal bases formed when one LTR is joined to another LTR. In the first full paragraph on page 29, the specification teaches that the connecting sequence of terminal bases formed when one LTR is joined to another LTR is typically about eight base pairs. As the claim is understood, the segment of DNA forming a region for controlling the expression of an integrase gene (*i.e.*, a promoter) must be comprised within the connecting sequence of approximately 8 terminal bases formed when one LTR is joined to another LTR, wherein the connecting sequence must also have the function of a retroviral integrase recognition region.

State of the prior art and level of predictability in the art: The art does not teach any promoters that could be comprised within the connecting sequence formed by conjoined LTR's, let alone a connecting sequence having both promoter activity and the function of a retroviral integrase recognition region. Further, the art, exemplified by Pereira *et al.* (2000) *Nucleic Acids Res.* 28: 663-668, teaches that the promoter regulatory elements found within retrovirus LTR's lie in the U3 and R regions (see especially Figure 1 and the caption thereto).

Amount of direction provided by the inventor and existence of working examples: The specification does not provide a single example of a vector wherein the segment of DNA forming a region for controlling the expression of an integrase gene is situated within the connecting sequence of terminal bases formed by two LTR's joined together. The promoter activity in the examples reduced to practice is surely from the LTR's themselves and not from the connecting sequence.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the relevant art and specification simply provide no guidance as to how one might construct a segment of DNA forming a region for controlling the expression of an integrase gene comprised within the connecting sequence of approximately 8 terminal bases formed when one LTR is joined to another LTR, wherein the connecting sequence also has the function of a retroviral integrase recognition region. Therefore, it would require undue experimentation to make the claimed plasmid vector.

Allowable Subject Matter

Claims 1 and 5-7 are allowed.

Conclusion

This application contains claims 16-18 drawn to an invention nonelected with traverse in the Paper filed 14 August 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DMS

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER